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Cancer and Breakthrough Pain's Impact on a Diverse Population

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ABSTRACT

Background. Although breakthrough pain (BTP; pain flares interrupting well-controlled baseline pain) is common among patients with cancer, its prevalence, characteristics, and impact on health-related quality of life (HRQOL) are poorly understood in ethnic minorities.

Methods. This comparative study examines ethnic and gender differences in BTP characteristics and impact on HRQOL. Patients with stage III or IV cancer of the breast, prostate, colorectal, or lung, or stage II–IV multiple myeloma with BTP completed surveys (upon initial assessment, 3 months, and 6 months) assessing consistent pain, BTP, depressed affect, active coping ability, and HRQOL.

Results. Respondents (N = 96) were 75% white, 66% female with a mean age of 56 ± 10 years. All subjects experienced significant psychological distress, but there were no racial differences in depression prevalence. Minorities reported significantly greater severity for consistent pain at its worst ($P = 0.009$), least ($P \leq 0.001$), on average ($P = 0.004$), and upon initial assessment ($P = 0.04$) as well as greater severity for BTP at its worst ($P = 0.03$), least ($P = 0.02$), and at initial assessment ($P = 0.008$). Although minorities reported more flare types (3.0 vs 1.8, $P = 0.001$), there were no significant ethnic differences in the duration, quality, or location of pain flares. Minorities consistently reported poorer outcomes on each HRQOL subscale (physical, role, emotional, cognitive, and social functioning) measured, although not statistically significant, as well as poorer QOL symptom control ($P = 0.08$) including lower dyspnea control ($P = 0.002$).

Conclusions. Overall, minorities experienced greater consistent and breakthrough pain as well as poorer HRQOL. These data suggest further health care disparities in the cancer and pain experience for minorities.

Key Words. Breakthrough Pain; Cancer Pain; Gender; Health Care and Health Policy; Physician Variability; Pain Management; Racial and Ethnic Disparities

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Introduction

Cancer pain (i.e., pain associated with cancer or its treatment) is common and significantly impairs health and quality of life (QOL). Pain is experienced by more than 60% of patients with cancer [1] and attributed to direct effects of the neoplasm, therapeutic interventions, and syndromes unrelated to the disease process [2]. Breakthrough pain (BTP; a transitory flare of moderate

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to severe pain, interrupting mild background pain being controlled by a stable analgesic regimen) is a common problem among patients with cancer and may lead to complicated clinical problems [3]. When BTP occurs, it may indicate more severe pain syndromes in patients with cancer while also predicting an inadequate response to analgesics [4]. Previous observational studies describing BTP's characteristics and treatment in the cancer population vary widely with prevalence estimates ranging from 19% [5] to 93% [6]. Zeppetella et al.'s study of patients with cancer admitted to a hospice facility found 89% presented with BTP [7]. Portenoy et al. described BTP's quality and characteristics while distinguishing it from other pain syndromes [7–9]. The existing literature indicates variability in BTP flares (lasting from seconds to hours) and the unpredictable quality (often described as sharp, dull, achy, lancinating, or burning) [7].

Pain is a feared symptom, and patients with cancer often believe it is a sign that their cancer has worsened [10,11]. Most patients with cancer attribute their BTP to tumor location and growth, while some believe that it is due to cancer treatment or causes unrelated to their disease process. Patients commonly report BTP occurs following a particular movement or at the end of a medication course (often referred to as end-of-dose failure) [9]. BTP's unpredictable onset and diverse pathophysiology pose unique challenges while yielding variability in how physicians manage BTP [9]. It is commonly treated with "rescue doses" of analgesics (including opioids) used for managing chronic cancer pain [9]. A clinically significant pain syndrome, BTP also impacts health-related (HRQOL) and mental well-being. When compared with individuals without cancer, patients with cancer have an increased prevalence of depressed mood and psychological distress resulting in decreased personal well-being and HRQOL [12]. Additionally, patients experiencing BTP have more psychological distress and lower HRQOL than the general cancer population [8]. Patients with cancer with BTP experience significantly more functional impairment, higher anxiety, and an increased prevalence of depressed mood than patients with cancer without BTP. Although many researchers have contributed to an understanding of BTP's characteristics and consequences, most studies fail to explore racial or gender differences [3].

Disparities in health and health care are well documented and remain a significant public health problem [13]. The Institute of Medicine's reports on health and health care disparities also document the unequal burden of cancer [13,14] while devoting minimal attention to pain. Overall, blacks have higher incidence and mortality rates for colorectal, lung, prostate, and breast cancer whites [14–19]. In addition, disparities in the prevalence, severity and treatment for all types of pain as well as structural barriers to pain care exist [20–22]. Minorities have a higher prevalence and more severe pain than non-Hispanic whites [23–26]. They are also less likely to have their pain complaints adequately assessed or documented in their medical chart [27]. Additionally, minority patients disproportionately receive inadequate analgesic therapy for their cancer pain and tend to report less satisfaction with pain treatment as well as less pain relief from pain medication when compared with non-Hispanic whites [10]. Even when treated, minorities experience additional barriers compared with non-Hispanic whites in accessing pain medications with pharmacies located in minority neighborhoods less likely to maintain adequate opioid analgesic supplies [28]. Likewise, the pain complaints of women receive less attention [29], and they are also at risk for suboptimal pain treatment than men. Overall studies attempting to examine gender-based differences in cancer pain are rare and reveal few differences in the severity of consistent pain. Although there is support for disparities in cancer pain treatment [30], gender-based differences in BTP have not been examined.

While there is evidence for racial and ethnic disparities in acute, chronic, and cancer pain care, previous research has not addressed potential disparities in BTP characteristics or QOL outcomes. We hypothesized that minorities with advanced cancer experienced greater consistent pain, more BTP episodes, and had worse HRQOL than whites. The current study seeks to enhance the existing literature by comparing BTP characteristics and QOL in ethnically diverse men and women. Additionally, this study sought to assess the impact of ethnicity or gender on BTP, HRQOL, and mental health.

Methods

Participants

Approval for this study was granted by the University of Michigan Health System Institutional Review Board (IRB) and the IRB Boards of the cooperating cancer centers. Written informed

consent was obtained from each subject upon study enrollment. The study involved collecting data from patients with cancer experiencing BTP with stage III or IV breast, prostate, colorectal or lung cancer, or stage II, III, or IV multiple myeloma. Subjects were identified at four urban outpatient cancer centers and through the University of Michigan Cancer Registry. English-speaking black, white, Hispanic, Arabic, and Native American patients between 18 and 75 years old were recruited for study participation. Only patients reporting BTP and receiving around-the-clock analgesic therapy for cancer pain were included in the study. An Eastern Cooperative Oncology Group Performance Status of ≤2 (no more than 50% of the day spent in bed) was required for inclusion such that highly impaired people were excluded from participating in the study. People ≥75 years old were excluded as their pain could be caused by other comorbid conditions. Medications and pain data were collected from participants upon recruitment.

Measures

Sociodemographics were assessed at screening (age in years as calculated from birth date, self-identified race, gender) and in the baseline survey. Marital status (never married, married, divorced, separated, widowed), education (≤6th grade, >6th grade but did not finish high school, high school diploma or equivalent, some college/trade school, college graduate or equivalent, graduate or professional school after college), employment (full-time employed, part-time employed, retired, voluntarily unemployed, involuntarily unemployed), and household income (≤$9999 or less, $10,000–30,000, $30,001–100,000, ≥$100,001) were all categorical variables. Cancer type and stage were also collected at screening and confirmed with the clinical database from the participating institution.

The Brief Pain Inventory (BPI) assessed pain severity and interference with normal physical and emotional functioning [31]. Items determined pain severity (pain at worst, least, average, and right now), pain-related interference (general, mood, walking, work, relationships, sleep, life enjoyment), pain characteristics (timing, duration, quality, cause), pain location (via two drawings of the body with instructions to shade areas with pain), medications, pain medication effectiveness, and an open-ended item regarding what actions relieved pain. Characteristics, location, pain medication effectiveness (0% to 100%), and a dummy variable for any activity effectively alleviating some portion of pain (0 = nothing helps, 1 = something can be performed to lessen pain) were used in analyses. The BPI severity items were used for both consistent and breakthrough pain with the following definitions preceding each section: "Your everyday, consistent pain is the pain for which your doctor(s) has prescribed pain medication(s) on a set daily regimen (for example, every 4–6 hours)" and "During periods of relatively consistent pain or periods that were relatively pain-free, you may have also experienced temporary flares of pain or pain attacks." Internal reliabilities for the items were 0.90 and 0.83, respectively, for the consistent and breakthrough pain scales. The remaining BPI items were asked in relation to consistent pain.

The Center for Epidemiological Studies Depression Scale (CES-D) assessed depressed affect. We dropped the four positively worded items from the original 20-item survey because factor analysis showed that the items do not accurately predict negative effect when reversed as confirmed in the literature [32,33]. The ordinal values of the remaining 16 items were summed and weighted to calculate an overall score comparable to the published scale range (0–60); scores >15 indicated severe psychological distress and depression. Internal consistency for the 16-item CES-D was consistent with published values ($\alpha = 0.91$) [32].

The John Henryism Active Coping Scale (JHACS) evaluated John Henryism, a high output active coping strategy characterized by protracted struggles against seemingly insurmountable obstacles. The construct was originally reported among aging African Americans and is correlated with high blood pressure and bodily pain. The sum score of 12 Likert-type items was calculated (1 = completely false; 5 = completely true; 60 = maximum active coping score). Internal consistency ($\alpha = 0.87$) of the JHACS was higher than previously published values [34].

The Barriers Questionnaire (BQ-II) assessed barriers in patient attitudes toward pain management and treatment. The BQ-II questionnaire has four separate subscales: physiological effects, fatalism, communication, and harmful effects [35]. Mean scores were calculated for each set of Likert-type subscales; fatalism items were reverse scored before analysis. The internal consistency of BQ-II subscales ranged from $\alpha = 0.60$ to 0.91. Only the fatalism subscale had a reliability value below its previously published value of $\alpha = 0.79$ [35]; in this sample, the reliability value was $\alpha = 0.60$. Our small sample size and the few questions on the

subscale may account for the difference in reliabilities, or it may be, as with the CES-D items, that some items have different meaning to patients with cancer.

The European Organization for the Research and Treatment of Cancer survey (EORTC QLQ-C30) assessed HRQOL [36]. Five QOL functioning domains (physical, role, cognitive, emotional, and social) and eight symptom-control domains (fatigue, pain, nausea, vomiting, dyspnea, anorexia, diarrhea, and constipation) were evaluated (frequency during the past week) for their contribution to QOL. Additional measures assessed financial concerns, global health, and overall QOL. All scores were linearly transformed to a 0–100 scale. Internal consistency of the EORTC subscales ($\alpha = 0.71$–0.91) was higher than previously published results [36].

Pain Management Measures

Several pain management measures were computed: 1) pain medication potency; 2) total number of medications taken; and 3) adequacy of pain management via the Pain Management Index (PMI). Using the World Health Organization guidelines for pain treatment, the PMI was computed by using a combination of patients' pain severity scores at worst during the past week and their current analgesic medication potency. The medicines were classified into 38 classes by three medical staff (two anesthesiologists and one PharmD) and then collapsed into four groups based on their analgesic function: 0 = nonanalgesic; 1 = nonopioid analgesic; 2 = weak opioid; 3 = strong opioid. Using these categories, an ad hoc procedure was used to classify patients' treatment into the identical four drug potency categories yielding the drug potency variable.

The pain severity score collected from the Mean BPI pain severity scale was collapsed into four categories: 0 = absence of pain (BPI severity ≤ 0.9); 1 = mild pain (BPI severity = 1.0–3.9); 2 = moderate pain (BPI severity = 4.0–7.9); and 3 = severe pain (BPI severity = 8.0–10.0). The PMI is the difference between the analgesic potency and the categorized pain level and ranges from –3 to +3. This ordinal variable was also used in its categorical form (0 = inadequate analgesic therapy [PMI = –3 to 0], 1 = adequate analgesic therapy [PMI = +1 to +3]).

Statistical Analysis

Descriptive statistics were calculated by using SPSS (SPSS Inc., Chicago, IL) 14.0. Analysis of variance (ANOVA) and chi-square analysis were used. Because of the limited sample size, findings with a two-tailed probability of type I error of $P \leq 0.10$ are reported to determine differences between whites and minorities and between men and women in sociodemographics, pain characteristics, and experiences, and for each QOL measure examined. Multiple analysis of variance (MANOVA) was used to examine differences between whites and minorities and between men and women in overall consistent pain, BTP severity, QOL functioning, and QOL symptom control, and the BQ-II subscales as the subscales for these measures are highly correlated. Correlations were also examined between consistent and breakthrough pain variables and other variables. ANOVA and MANOVA techniques are relatively robust in terms of assumptions of normality. Additionally, for the 36 continuous or ordinal variables used in the analyses, only 1 had a skewness of >2 (number of pain sites). Most (83%) variables had skewness of 1, including all BPI subscales and all the EORTC subscales except nausea and diarrhea. The combined measures were all normally distributed. Recognizing that inter- and intrarace variability exists for all races, a post hoc analysis was performed to verify that the results would not differ if comparisons were made for whites vs blacks (the only subgroup large enough for comparison).

Results

Demographics

Ninety-six subjects (blacks [N = 19], whites [N = 68], Hispanic [N = 3], Arabic [N = 2], and Native Americans [N = 4], including 1 biracial person counted in both categories) completed the baseline survey (71% white [24–75 years, N = 68], 29% minority [30–75 years, N = 28], 66% female). This racial breakdown is consistent with Michigan's population breakdown overall. There were no significant differences between the white and minority sample in age, sex, or education. There were significant differences in marital status between the two groups, with whites more likely to be married (73% vs 29%) and less likely to be divorced (19% vs 33%) than minorities ($P = 0.001$). There were also differences in annual household income, with whites more likely to fall into the high-income group (≥$100,000) than minorities ($P = 0.04$). Women were significantly less likely than men to be married (50% vs 84%, $P = 0.01$), and there is a trend for women to be in

Table 1 Sociodemographic characteristics for the sample

	Total N (%)	White N (%)	Minority N (%)	Difference *P* value
N	96	68 (71)	28 (29)	
Age (years)	56.5	57.3	54.3	0.09
% Men	33 (34)	20 (29)	13 (46)	0.11
Education				
Less than high school	14 (15)	10 (15)	4 (14)	0.18
High school graduate	32 (33)	21 (31)	11 (39)	
Some college	25 (26)	21 (31)	4 (14)	
≥College graduate	25 (26)	16 (24)	9 (32)	
Employment				0.41
Full time	12 (14)	7 (11)	5 (20)	
Part time	7 (8)	4 (6)	3 (12)	
Retired	39 (44)	27 (43)	12 (48)	
Voluntarily unemployed	14 (16)	12 (19)	2 (8)	
Involuntarily unemployed	16 (18)	13 (21)	3 (12)	
Income				0.08
$9,999 or less	12 (13)	6 (9)	6 (22)	
$10,000–$30,000	32 (34)	20 (30)	12 (44)	
$30,001–$100,000	42 (45)	35 (53)	7 (26)	
>$100,000	7 (8)	5 (8)	2 (7)	
Marital status				
Never married	8 (9)	4 (9)	4 (14)	0.002
Married	58 (62)	49 (74)	9 (32)	
Divorced/separated	22 (23)	11 (17)	11 (39)	
Widowed	6 (6)	2 (3)	4 (14)	
Cancer type				
Breast	31 (33)	24 (35)	7 (26)	0.72
Colon	14 (15)	8 (12)	6 (22)	
Lung	27 (28)	20 (29)	7 (26)	
Multiple myeloma	20 (21)	14 (21)	6 (22)	
Prostate	3 (3)	2 (3)	1 (4)	
Primary cancer stage†				
II (multiple myeloma only)	5 (6)	2 (3)	3 (13)	0.29
III	47 (52)	32 (50)	15 (63)	
IV	38 (42)	30 (47)	8 (33)	

* $P \leq 0.05$.
† Differences in primary cancer stage, with white Americans more likely to have a stage IV diagnosis and less likely to have a stage II diagnosis, may be due to the fact that multiple myeloma was more common among the minority sample.

lower-income groups ($P = 0.06$). Table 1 provides additional sociodemographic information for the sample.

Cancer Differences

Although there were no significant differences between whites and minorities in primary cancer diagnosis location, there was a trend level difference in primary cancer stage ($P = 0.09$). Compared with minorities, whites had a higher frequency of stage IV cancer (whites = 43%, minorities = 29%) and a lower frequency of stage II cancer (whites = 2.8%, minorities = 16.7%). Although the differences were not statistically significant, it appears that the mean subject age at first primary cancer diagnosis may be different between whites and minorities for breast cancer and multiple myeloma. In both instances, minorities were diagnosed at younger ages. Women were more likely to have a diagnosis of breast cancer, but, when breast cancer is removed from the diagnostic spectrum, there are no differences by gender in prevalence of other cancers.

Consistent Pain

The most common pain locations were nonmidline back (36%), spine (31%), and legs (28%). Although there were no significant differences in the number of pain locations, minorities experienced pain more often than whites in the nonmidline back (54% vs 29%, $P = 0.03$), upper nonmidline back (32% vs 15%, $P = 0.05$), lower nonmidline back (36% vs 12%, $P = 0.006$), arm and shoulder (32% vs 16%, $P = 0.08$), and head (14% vs 1%, $P = 0.01$). Women experienced more spine pain than men (37% vs 18%, $P = 0.06$).

Minorities reported significantly higher pain scores for consistent pain than whites (multivariate $F = 5.49$; $P = 0.001$). Minorities also had significantly higher scores on the interference scales (multivariate $F = 2.36$; $P = 0.03$) than whites. Consistent pain and pain interference were not statistically different by gender, although further examination shows that, in every case, the mean interference was higher for women. Figure 1 shows mean scores on the four consistent pain measures by ethnicity. Table 2 shows consistent pain, BTP, and pain interference by race/ethnicity and gender. The mean PMI of –1.01 suggests that most subjects were prescribed adequate pain medications (range = –3 to +3; negative numbers reflecting medication stronger than pain strength and positive numbers reflecting pain stronger than medication). When PMI was examined as a continuous variable, there were no ethnic or gender differences in medication strength or subject-reported consistent pain relief received from medication (62% relieved overall). Further examination of the dummy variable for "adequate" vs "inadequate" medication showed that only women (N = 6) were prescribed inadequate pain medication, a trend level difference ($P = 0.07$). Pain interference was also a significant issue for subjects with mean interference ranging from 3.6 (relationships) to 5.5 (work) on a scale of 0 to 10. Minorities had higher interference scores on general activity, mood, walking, relationships, and enjoyment of life. There were no significant gender differences in interference.

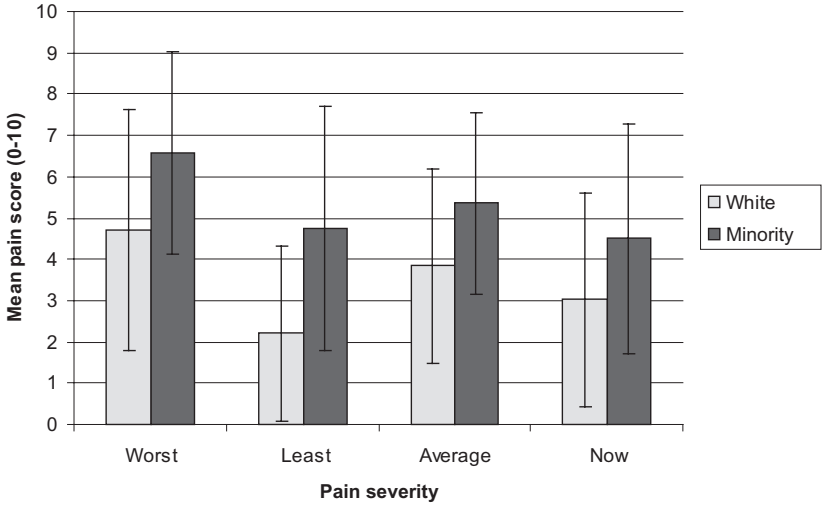

Figure 1 Consistent pain by ethnicity ($P < 0.05$ for all pairs).

BTP

BTP history was required for study inclusion, but variability in BTP characteristics was noted. On average, subjects experienced BTP for 619 days, with BTP duration ranging from 0 to 168 months. There were no differences between whites and minorities or men and women in BTP duration or in the number of BTP episodes experienced on average per week. Subjects attributed the precipitating event for BTP to several causes (e.g., movement, end-of-pain medication course), but there were no differences by ethnicity in the frequencies of precipitating events. Although there was great variability within each group, there were not significant ethnic or gender differences in the ability to predict BTP onset. Overall, most subjects (79%) reported BTP could be at least partially palliated (most commonly through medications). Subjects also reported only 62% of the BTP they experienced was relieved by medication and by using other methods for reducing BTP (e.g., lying down, limiting movement, and heating pads). There were not significant ethnic or gender differences in BTP placability or in strategies used for pain relief.

BTP was higher for minorities but not significantly different (multivariate $F = 2.08$; $P = 0.08$) and did not differ by sex (multivariate $F = 1.63$; $P = 0.16$). There were significant ethnicity differences on four out of five BTP subscales, with minorities reporting significantly higher BTP

Table 2 Consistent pain, breakthrough pain, and pain interference by ethnicity and gender

	White	Minority	Multivariate F	*P*	Men	Women	Multivariate F	*P*
Consistent pain			5.49	0.001			0.29	0.880
Worst	4.71 ± 2.93	6.57 ± 2.44		0.004	5.34 ± 3.17	5.21 ± 2.79		0.839
Least	2.21 ± 2.12	4.75 ± 2.95		<0.001	2.81 ± 2.91	3.03 ± 2.53		0.705
Average	3.84 ± 2.35	5.36 ± 2.20		0.004	4.16 ± 2.70	4.35 ± 2.25		0.713
Right now	3.03 ± 2.59	4.50 ± 2.77		0.015	3.47 ± 2.78	3.46 ± 2.70		0.989
Breakthrough pain			2.08	0.08			1.63	0.163
Worst	6.93 ± 2.23	8.11 ± 1.83		0.018	6.90 ± 2.66	7.52 ± 1.85		0.210
Least	3.27 ± 2.28	4.44 ± 2.74		0.041	3.10 ± 2.47	3.93 ± 2.46		0.140
Average	4.98 ± 2.22	5.81 ± 2.51		0.125	4.67 ± 2.48	5.55 ± 2.21		0.093
Right now	2.95 ± 2.49	4.70 ± 2.92		0.005	3.37 ± 2.75	3.57 ± 2.76		0.744
Most recent	6.73 ± 2.40	8.04 ± 1.81		0.014	6.37 ± 2.88	7.55 ± 1.82		0.022
Interference			2.36	0.031			0.53	0.810
General activity	4.02 ± 3.05	6.31 ± 3.07		0.002	4.74 ± 3.28	4.68 ± 3.22		0.936
Mood	3.79 ± 3.23	5.92 ± 3.31		0.006	4.15 ± 3.11	4.54 ± 3.51		0.617
Walking ability	3.90 ± 3.35	5.81 ± 3.39		0.018	4.30 ± 3.07	4.54 ± 3.64		0.761
Work, in and out of home	5.26 ± 3.32	6.31 ± 3.36		0.181	5.37 ± 3.22	5.66 ± 3.42		0.714
Relations with others	3.03 ± 2.84	4.85 ± 2.60		0.014	2.93 ± 3.14	3.85 ± 3.17		0.208
Sleep	4.90 ± 3.35	6.27 ± 3.03		0.076	5.00 ± 3.46	5.44 ± 3.24		0.565
Enjoyment of life	4.81 ± 3.45	6.73 ± 2.97		0.015	5.07 ± 3.13	5.51 ± 3.55		0.585

* Statistically significant result ($P \leq 0.05$).

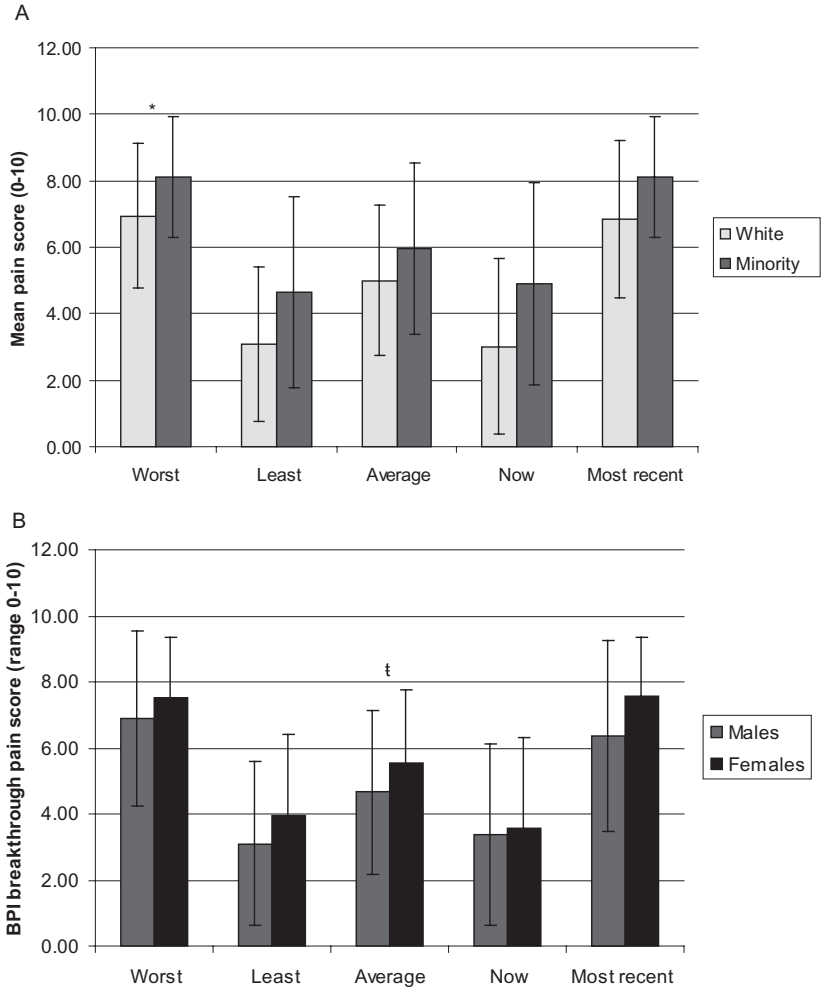

Figure 2 Breakthrough pain by ethnicity (A) ($P < 0.05$ except pain at least) and gender (B). BPI = Brief Pain Inventory.

scores than whites at its worst ($P = 0.02$), least ($P = 0.04$), when the survey was administered ($P = 0.005$), and most recently ($P = 0.01$). Women reported their BTP on average ($P = 0.09$) was worse, and their most recent pain flare was stronger (7.6 vs 6.4, $P = 0.02$). Figure 2 shows BTP by ethnicity and by gender. Minorities also experienced a significantly greater number of different types of pain flares than whites (3.0 vs 1.8, $P = 0.001$). Minorities experienced BTP in the legs at a higher frequency than whites (37.5% vs 16.7%; $P = 0.03$), but there were not significant differences between the two populations in the incidence of BTP at other sites on the body or in the total number of pain locations. There was also great variability in BTP quality, with subjects most commonly reporting pain that was aching (27.9%), sharp (23.5%), or throbbing (14.7%), although there were no ethnic or gender differences. PMI for BTP was not different by race/ethnicity or gender.

QOL, Depression, Coping Strategies, and Comorbidities

F values for the MANOVA tests of each set of subscales were not significant, although when all symptoms subscales were combined into a single "Symptom" scale, there were trend level differences ($P = 0.08$) between the scores of whites and minorities. Whites and minorities demonstrated statistical similarities on the functioning scales of the EORT-C. Although not statistically significant, minorities had consistently poorer outcomes on each subscale and had poorer functioning at a trend level ($P = 0.08$) on the social functioning scale. Minorities also reported higher average scores on each QOL symptom control subscales than whites, but only the pain and dyspnea symptom control subscales demonstrated statistically significant differences between the two groups ($P = 0.05$). There were trend level differences between whites and minorities in financial difficulty ($P = 0.09$). The functioning subscales showed no gender or ethnic

Table 3 Functioning and Symptoms as Measured by the EORTC

	White	Minority	Multivariate F	*P*	Men	Women	Multivariate F	*P*
EORTC functioning scales			0.62	0.71			0.99	0.43
General health	54.2 ± 24.9	51.59 ± 27.5	0.16	0.69	55.0 ± 25.2	52.7 ± 25.8	0.15	0.70
Physical	61.8 ± 22.7	59.05 ± 26.0	0.21	0.65	64.4 ± 24.9	59.3 ± 22.6	0.95	0.33
Role	49.0 ± 28.5	46.83 ± 32.3	0.08	0.77	47.2 ± 30.7	49.1 ± 28.8	0.08	0.78
Emotional	63.3 ± 25.7	59.1 ± 32.0	0.37	0.55	63.1 ± 29.3	61.8 ± 26.3	0.04	0.84
Cognitive	66.4 ± 25.6	64.3 ± 30.9	0.10	0.76	63.3 ± 32.3	67.3 ± 23.6	0.42	0.52
Social	52.3 ± 32.8	38.1 ± 29.4	3.13	0.08	44.4 ± 33.4	51.2 ± 31.9	0.85	0.36
EORTC symptom scales			0.97	0.46			0.84	0.57
Fatigue	58.8 ± 24.1	62.7 ± 24.4	0.48	0.49	64.3 ± 26.3	57.3 ± 22.6	1.81	0.18
Nausea/vomiting	22.5 ± 27.0	24.7 ± 30.9	0.11	0.74	24.8 ± 31.8	22.1 ± 25.8	0.18	0.67
Pain	54.6 ± 25.2	66.7 ± 25.9	4.12	0.05	55.6 ± 28.8	59.2 ± 24.2	0.41	0.52
Trouble sleeping	58.6 ± 29.8	68.0 ± 34.0	1.67	0.20	63.6 ± 32.7	59.8 ± 30.4	0.32	0.57
Appetite	39.9 ± 36.1	45.3 ± 35.8	0.41	0.52	47.5 ± 39.1	37.9 ± 33.9	1.49	0.23
Shortness of breath	29.8 ± 32.1	45.3 ± 38.3	3.81	0.05	33.3 ± 38.2	34.5 ± 32.4	0.02	0.88
Constipation	36.4 ± 35.4	48.0 ± 36.1	1.94	0.17	39.4 ± 38.6	39.7 ± 34.5	0.00	0.97
Diarrhea	14.7 ± 25.6	20.0 ± 23.6	0.83	0.37	13.1 ± 23.5	17.8 ± 25.9	0.74	0.39
Financial difficulties	45.3 ± 38.8	63.0 ± 38.5	4.02	0.05	39.6 ± 36.4	55.9 ± 39.9	3.75	0.06
CES-D								
Depression	21.5 ± 13.3	25.7 ± 14.0	1.94	0.17	21.4 ± 14.2	23.4 ± 13.3	0.50	0.48
Barriers questionnaire			1.75	0.15			0.67	0.61
Physical	1.8 ± 1.1	2.0 ± 1.4	1.01	0.32	1.81 ± 1.18	1.91 ± 1.23	0.50	0.48
Fatalism	1.4 ± 1.1	1.5 ± 1.1	0.57	0.45	1.33 ± 1.04	1.53 ± 1.07	0.70	0.41
Communication	1.0 ± 1.0	1.4 ± 1.3	1.60	0.21	1.04 ± 1.06	1.26 ± 1.17	0.59	0.44
Harmful side effects	1.9 ± 1.2	2.5 ± 1.5	4.40	0.04	1.98 ± 1.31	2.28 ± 1.28	1.54	0.22
John Henryism active coping	47.4 ± 6.7	48.4 ± 10.9	0.30	0.59	50.1 ± 6.1	46.4 ± 8.8	4.72	0.03
Comorbidities	2.1 ± 1.7	2.5 ± 2.5	0.77	0.38	2.3 ± 2.1	2.2 ± 1.9	0.07	0.79

EORTC = European Organisation for Research and Treatment of Cancer; CES-D = Center for Epidemiological Studies Depression Scale.

differences when the function domains were combined into a single "Function" scale. Table 3 shows means and standard deviations by subgroup on the EORTC subscales.

The subjects experienced significant psychological distress and depression when measured with the CES-D (mean = 22.5; maximum possible score = 60, and scores > 16 indicate depression), but there were no differences by ethnicity or gender. Barriers to pain treatment were not significantly different overall (multivariate $F = 1.75$; $P = 0.15$ by ethnicity, $F = 0.67$, $P = 0.61$ by sex), although minorities perceived more harmful side effects of medications than whites ($P = 0.04$). All participants scored highly on the JHACS (mean = 47.6, maximum possible score = 60), and there were not significant ethnic differences, although men had higher scores than women ($P = 0.03$). When the subjects were asked if they had ever been diagnosed by a physician with any of 19 different comorbidities, there were no ethnic or gender differences in the sum of comorbidities, although there was a significant difference between whites and minorities in chest pain and angina frequency ($P = 0.03$) when comorbidities were examined individually. Men were more likely to have been told they have high blood pressure ($P = 0.04$) and there was a trend for women to have rheumatism or arthritis more frequently ($P = 0.08$).

The Relationship Between Pain and Quality of Life

Bivariate correlations between the four consistent pain measures and the five BTP measures of the BPI and quality of life measures showed strong correlations (Table 4). For functioning, both consistent and breakthrough pain were correlated with general health, physical and role functioning, and, to a lesser degree, with emotional, cognitive, and social functioning. Both types of pain measures were also associated with all symptom scales except diarrhea. Depression as measured by PTSD was the only one where BTP had a more pervasive relationship than consistent pain, yielding four significant correlations compared with two.

Post Hoc Analysis

When whites were compared with blacks, analyses looked nearly identical to those performed with all racial and ethnic minorities collapsed into the minority group.

Discussion

The existing evidence indicates ethnic and gender disparities in the prevalence, severity, and

Table 4 Correlations between pain variables and quality of life outcomes

	Consistent Pain				Breakthrough Pain				
	Pain at Worst	Pain at Least	Pain on Average	Pain Right Now	Pain at Worst	Pain at Least	Pain on Average	Pain Right Now	Most Recent
Functioning									
General health	**–0.22***	**–0.36*****	**–0.21***	**–0.34*****	–0.07	**–0.25***	**–0.23***	**–0.37*****	**–0.23***
Physical	**–0.43*****	**–0.47*****	**0.46*****	**–0.48*****	**–0.22***	**–0.43*****	**–0.35*****	**–0.49*****	**–0.23***
Role	**–0.39*****	**–0.37*****	**–0.41*****	**–0.33****	**–0.22***	**–0.39*****	**–0.28****	**–0.38*****	**–0.28****
Emotional	–0.09	**–0.24***	–0.12	–0.11	–0.07	**–0.22***	–0.17	*–0.20*	–0.17
Cognitive	–0.16	*0.18*	–0.12	**–0.21***	–0.05	*–0.17*	–0.13	**–0.22***	*–0.18*
Social	*–0.17*	*0.18*	*–0.17*	**–0.26****	–0.10	–0.15	**–0.25***	**–0.31****	–0.09
Symptoms									
Fatigue	**0.23***	**0.24***	**0.25***	**0.29****	*0.19*	**0.31****	**0.28****	**0.31****	*0.20*
Nausea/vomiting	**0.29****	**0.40*****	**0.38*****	**0.36*****	0.14	**0.39*****	**0.32**	**0.26***	0.13
Pain	**0.66*****	**0.59*****	**0.64*****	**0.65*****	**0.46*****	**0.45*****	**0.50*****	**0.68*****	**0.53*****
Trouble sleeping	*0.18*	**0.34*****	**0.26****	**0.30****	0.16	**0.38*****	*0.19*	**0.29****	*0.18*
Appetite	**0.40*****	**0.35*****	**0.36*****	**0.40*****	*0.20*	**0.31****	**0.22***	**0.35*****	*0.20*
Shortness of breath	**0.23**	**0.21***	*0.17*	**0.28****	0.17	**0.24***	0.11	**0.26***	**0.22***
Constipation	**0.27****	*0.20*	*0.18*	**0.23***	**0.28****	**0.31****	**0.23***	**0.33****	**0.30****
Diarrhea	0.09	0.15	0.12	0.12	0.03	0.16	0.14	0.09	0.16
Financial difficulties	0.12	*0.17*	0.12	0.14	0.10	0.11	0.12	**0.23***	0.13
Barriers to treatment									
Physiological	0.12	**0.30****	*0.17*	0.10	–0.04	**0.22***	**0.20***	*0.19*	0.12
Fatalism	0.15	**0.23***	**0.25***	**0.25***	0.07	0.15	0.04	**0.23***	0.10
Communication	*0.17*	**0.26***	0.15	**0.24***	0.05	0.11	0.13	**0.33****	0.16
Harmless effects	0.15	**0.28****	**0.21***	0.03	–0.02	0.16	0.07	0.12	0.09
Mental health/coping									
Depression (CES–D)	0.16	**0.26****	**0.20***	0.16	0.17	**0.30****	**0.29****	**0.24***	**0.27****
John Henryism	–0.12	0.04	–0.14	–0.12	–0.08	*–0.18*	–0.15	–0.14	–0.04
Comorbidities	**0.21***	0.02	0.10	*0.18*	0.04	–0.04	–0.03	0.08	0.03

Italics $P \leq 0.10$. * $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.001$.
CES-D = Center for Epidemiological Studies Depression Scale.

treatment of acute, chronic, and cancer pain [20,37–40]. Minorities may also report more severe pain and greater pain-related interference with daily physical and emotional functioning [20,23,24]. Similarly, gender-based differences are documented, with women reporting higher prevalence of most pain syndromes than men [41]. Barriers to treatment exist for minority populations and women even when they are assessed and treated for pain complaints [41]. Minorities also face structural barriers in accessing pain medications with pharmacies in predominantly minority neighborhoods being less likely to carry adequate supplies of prescription analgesics [28]. In addition, while Miaskowski and others did not find disparities in the severity of cancer pain by gender, disparities in treatment were identified [30]. However, it is important to note that Miaskowski and others did not examine BTP [30]. Portenoy et al. brought national attention to BTP's impact on QOL but did not examine ethnic or gender variations and implications in the experience [8]. While there is compelling research demonstrating ethnic- and gender-based disparities in acute, chronic, and cancer pain, there is minimal information assessing BTP characteristics and its impact on HRQOL in an ethnically diverse population of men and women [8,20]. To our knowledge, this is one of the first to examine both ethnic and gender differences in BTP characteristics and HRQOL. We found that minorities experienced significantly more consistent pain, BTP, and had diminished QOL than whites while women experienced higher levels on some BTP measures and less adequate pain management than men.

As previously illustrated, BTP characteristics were highly variable. Our results confirm previous research documenting racial and ethnic differences in consistent cancer pain with minority populations reporting more severe consistent pain and more pain-related interference [20]. An important new finding is that minorities also reported more BTP than whites. Likewise, our findings were consistent with earlier findings showing no gender-based disparities in consistent cancer pain [30]. We extend the literature by showing some BTP measures differed by gender. However, the etiology of these ethnic and gender differences in consistent and breakthrough pain remains unclear. Important considerations include clinician variability in assessing and treating pain in these populations. This is consistent with litera-

ture revealing an unequal burden of pain and clinician variability in decision making for all types of pain [20,23,24]. For instance, Bernabei et al. showed minorities are less likely to have their pain complaints recorded in their medical chart and received lesser quality treatment even when assessed [27]. Clearly, clinician variability in pain management decision making as well as structural barriers to quality pain care is well documented and may influence pain severity [28]. Although examining physician decision making was not an aim, future studies examining the prevalence of BTP and consistent pain in diverse populations with cancer should attempt to do so.

Beyond clinician variability, patient variability must also be considered when interpreting our findings [42,43]. Consistent with existing research documenting accelerated aging in minority populations, minorities were diagnosed with breast cancer and multiple myeloma at younger ages than whites. Trend level ethnic differences in primary cancer stage were also identified, with minorities more likely to have a stage II cancer diagnosis and less likely to have a stage IV diagnosis. These differences were most likely due to our decision to include multiple myeloma, the only diagnosis where patients in stage II were recruited and a diagnosis more frequent in minorities. Cleeland, Anderson, and others, demonstrated in ethnically diverse populations how patient preferences and attitudes about cancer and pain play a significant role in their willingness to report pain and to seek treatment [10,11]. Our finding that minorities reported more barriers related to medication side effects offers another explanation for increased pain severity. Meghani and Keane noted several reasons for ethnic differences in medication use for treating cancer pain, including analgesic side effects, meaning attributed to pain, and fears of dependency [44]. Such differences may exist by gender and appear to differ by pain cause [45–47]. Thus, when considering cancer pain, future longitudinal studies should examine BTP in a late-stage cancer population while specifically addressing patient preferences and attitudes in both reporting and seeking pain care.

Another striking finding was, although few were statistically significant, minorities reported consistently poorer scores on all functioning and symptom control subscales of the EORTC than whites. The literature suggests that appropriate pain management can lead to dramatic improvements in both overall pain and HRQOL [48–50]. When consistent and breakthrough pain scores are analyzed, our results suggest that minorities experienced more pain. Minorities also reported poorer QOL symptom control, with significant differences in dyspnea control and pain control. Ethnic differences on the pain control subscale were also consistent with higher pain scores reported by minorities for both consistent and breakthrough pain. Also interesting was the finding that, when all symptom control subscales were combined into a single scale, there were trend level, but not statistically significant, differences between whites and minorities. This suggests that minorities do not experience the same level of symptom control as whites do. We found poor QOL symptom control among minorities, consistent with literature citing disparities in pain treatment and for other conditions as well [13]. The strong correlations found between pain and QOL scales support this case. To our surprise, no statistical differences were found on any QOL functioning subscales except the social functioning (a trend level difference), although average scores for minorities were lower on each subscale than for whites. Additionally, higher pain levels did not translate to poorer functioning, and this observation deserves further study. We also observed differences in financial difficulties in the QOL survey consistent with lower annual household incomes reported by minorities and by women. Future studies should examine whether and how financial difficulties correlate with health insurance.

Although all groups had clinically important depressive symptoms and psychological distress when examining psychological impairment via the CES-D, we did not find significant ethnic or gender differences. Consistent with the cancer literature, we observed a high prevalence of depression in our sample [1]. The literature also provides evidence for pain causing sleep disturbance and depression [1]. Both the cancer and the palliative care literature provide evidence for depression as a normal stage [51–53], while the chronic pain literature provides evidence for increased depression and PTSD, in response to pain, in general, and for minorities, in particular [23,24]. However, when a patient is presenting with a cancer and a pain diagnosis, it is unclear whether pain causes depression, if cancer causes depression, or if there is another pathway yet to be examined. As all groups were equally depressed and we did not examine whether the subjects previously experienced clinical depression or chronic pain, it is unclear whether depression was a consequence of cancer or pain. Future studies should attempt to disentangle both

cancer and pain's impact on depression using a longitudinal design.

Maladaptive coping strategies diminish QOL and the ability to cope with significant illnesses. When James introduced the concept of John Henryism, it was strongly associated with blacks [34]. When analyzing JHACS, John Henryism was prevalent among the entire study population, although significantly higher among men. Exploratory examination did not find that John Henryism moderated the relationship between gender and the two statistically different BTP variables. Thus, it is plausible that men used this coping strategy for challenges posed by their cancer, rather than dealing with consistent or BTP syndromes. The lack of ethnic differences was surprising but suggests, when faced with a life-threatening illness, John Henryism may be a common coping strategy among patients with cancer regardless of race or ethnicity. As John Henryism has primarily been studied in blacks, until other studies addressing the validity of JHAC in other populations are available, this must be considered a potential study limitation. In addition, future studies should seek to confirm our findings and to examine whether John Henryism is an adaptive or maladaptive coping strategy when used in an ethnically diverse population with end-stage cancer and pain.

Although this study provides many significant implications for improving health and QOL in patients with cancer, there are potential limitations. First, the small sample size used for data analysis (particularly in the minority sample) may have limited the ability to find statistical differences between whites and minorities on many QOL measures and on comparing BTP characteristics. It is conceivable that these differences in the combined symptom-control scale and on individual subscales represent differences that could become statistically significant in a larger population. This, in combination with the consistency of all variables showing poorer outcomes for minorities, suggests that the noted differences represent significant disparities on a population level. These findings further suggest the need for more study in a larger diverse population. Second, self-report and nonresponse bias must be considered, although the surveys were completed privately and kept confidential. In particular, those people who were suffering most were less likely to agree to participate in the survey because they did not feel well. Finally, differences in incomes were noted, although there were no education differences noted between the minority and white samples. As subjects were recruited through cancer care facilities, our results may only reflect those with access to care and may not be representative for those with limited access to care.

These results have critically important implications for both clinical practice and health policy. We showed, when treating consistent pain and BTP, inadequate relief from pain medications for baseline or consistent pain. We extend the literature by confirming this in ethnically diverse men and women. Specifically, minorities experienced significantly more symptoms than whites in BTP severity and consistent pain severity, while women experienced more BTP on two measures. These findings are clinically important and significant regardless of ethnicity or gender while pointing toward important disparities in the quality of pain care (i.e., pain assessment and management) influencing overall health and well-being. In addition to minorities reporting higher consistent pain and BTP scores, they also had lower (but not significantly different) HRQOL than whites. This study provides new and critically important insights into ethnic- and gender-based disparities in health, pain care, and cancer care while serving as a novel model for future research addressing disparities in BTP on a population level.

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